REMARKS

Specification

The objection to the specification has been obviated by amendment.

Claims

Claims 18-25, 28 and 39-58 were pending in this application. Claim 28 has been amended. Support for amended claim 28 can be found at least, for example, at paragraph [057]. Accordingly, upon entry of this amendment, claims 18-25, 28 and 39-58 will be pending in this application.

Cancellation of and/or amendments to the claims should in no way be construed as acquiescence to any of the Examiner's rejections and were done solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the instant or in another patent application(s).

Rejection of Claims 18, 21-25 and 28 Under 35 U.S.C. §103(a)

The Examiner has maintained the rejection of claims 18-25 and 28 under 35 U.S.C. §103(a) as being unpatentable over Fischer et al. (US Pat. 6,939,543) in view of Patti (US Pat. 6,703,025). According to the Examiner, "because Fischer et al. teach antibodies directed to lipoteichoic acids 'can block the binding of Gram positive bacteria to epithelial cells...and Patti et al. teach ribitol phosphate is immunogenic and induces antibodies directed to S. aureus LTA[, i]t is obvious to make a monoclonal antibody to an antigen for which polyclonal antibodies have been made."

The test for *prima facie* obviousness is consistent with the legal principles enunciated in *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007). *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356 (Fed. Cir. 2007). "While the *KSR* Court rejected a rigid application of the teaching, suggestion, or motivation ("TSM") test, the Court acknowledged the importance of identifying 'a ***reason*** that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination." *Id.* (quoting *KSR*, 127 S. Ct. at 1731) (emphasis added). Although the TSM test should not be applied in a rigid manner, it can provide helpful insight to an obviousness inquiry. *KSR*,

127 S. Ct. at 1731. The *KSR* Court upheld the secondary considerations of non-obviousness, noting that there is "no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis." *Id.* Although the prior art reference, or references when combined, need not teach or suggest all of the claim limitations, a *reason* must be given why the differences between the prior art and the claimed limitation would have been obvious to one of skill in the art (see Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103, Federal Register, Vol. 72, No. 195).

The claims presently under examination are directed to pharmaceutical compositions comprising a therapeutically effective amount of a monoclonal antibody or an antigen binding fragment thereof that specifically binds to ribitol phosphate wall teichoic acid (WTA) of *S. aureus,* wherein said therapeutically effective amount of said antibody or fragment thereof alleviates or blocks colonization or infection by *S. aureus* upon administration to a patient.

The Examiner states that "Fischer teaches and suggests combination compositions of antibodies directed to ribitol phosphate and glycerol phosphate." Applicants respectfully submit that this statement mischaracterizes the teachings of Fischer. Specifically, Fischer (at column 5, lines 34-36) merely *defines* teichoic acids according to the dictionary definition that teichoic acids are polymers of either glycerol or ribitol phosphate. With respect to antibodies to teichoic aid, however, Fischer specifically states that *"[t]he teichoic acids related to this invention are **lipoteichoic acids which are acids made up of glycerol phosphate***" (see column 5, lines 40-43) (emphasis added). Therefore, the Examiner's assertion that "Fischer et al describe combination compositions of antibodies for antibody therapy...and obtain the combination composition of antibodies by immunization of mixtures of antigens to include both types of teichoic acid antigens" is unfounded.

The teachings of Patti *et al.* are concerned with the use of MSCRAMMs or antibodies thereof in multicomponent vaccines. The reference discloses that ligand binding domains in MSCRAMMs are defined by relatively short contiguous stretches of amino acid sequences (motifs) (see Column 2, lines 55-58). In addition to being directed to *protein* components of organisms rather than non-protein components (such as teichoic acids), the reference states that in "[t]o generate an effective immunotherapeutic against *S. aureus,* the vaccine must be multi-component and contain antigens that span the growth cycle as well as include antigens that are expressed by a majority of *S. aureus* isolates." (see Column 6, lines 31-35). Specifically, with respect to teichoic acids, the reference simply states that

> Teichoic acids, lipoteichoic acid for example, which are polymers of glycerol or ribitol phosphate, are linked to the peptidoglycan and can be antigenic. Antiteichoic antibodies are detectable by gel diffusion may be found in patients with active endocarditis due to *S. aureus.*

(see column 22, lines 48-52). In this passage, Patti *et al.* simply note that antiteichoic antibodies may be detected in some patients, however, it is unclear whether antibodies to lipoteichoic acid ("LTA") or ribitol wall teichoic acid ("WTA") are detectable, as the definition of "teichoic acids" in the passage includes both LTA and WTA. In fact, nowhere does Patti *et al.* clarify that ***anti-WTA antibodies, i.e., antibodies specific for teichoic acids which are polymers of ribitol phosphate,*** are detectable in patients with active endocarditis. Thus, the conclusion reached by the examiner that "Patti et al [shows] that ribitol phosphate is immunogenic, and induces antibodies, wherein polyclonal antibodies to ribitol phosphate have been made" cannot be inferred from the reference.

Furthermore, and as set forth in the previous reply, the only reference to monoclonals antibodies relates ***specifically to antibodies specific for MSCRAMM peptides***, not to antibodies that bind to any type of teichoic acid, let alone to WTA. The reference further fails to provide any suggestion that antibodies to teichoic acid provide for increase opsonization and phagocytosis.

Applicants teach that blocking of wall teichoic acid (WTA), complex suface-exposed polymers covalently linked to peptidoglycan, is sufficient to reduce nasal colonization of *S. aureus* in an animal model. Importantly, this was the *first demonstration* of a staphylococcal factor, in this case a non-peptide factor, that is necessary for nasal colonization. The claims are directed to pharmaceutical compositions comprising a therapeutically effective amount of a monoclonal antibody or an antigen binding fragment thereof that specifically binds to ribitol phosphate wall teichoic acid (WTA) of *S. aureus,* wherein said therapeutically effective amount of said antibody or fragment thereof alleviates or blocks colonization or infection by *S. aureus* upon administration to a patient. None of the art of record teaches or suggests that any amount of an antibody, let alone an antibody which binds to WTA, would be therapeutically effective to alleviate or block colonization or infection by *S. aureus.* Patti *et al.* teach that in order to be therapeutically effective, protein MSCRAMMS on the surface of staphylococci must be blocked and preferably, multiple staphylococcal components must be blocked (see, *e.g.,* column 6, lines 31-35). Accordingly, the reference actually teaches away from the use of antibodies against a single, non-peptidic component of

staphylococci as a therapy which is effective to block colonization or infection with *S. aureus* in a patient.

As set forth above, neither Fischer *et al.* nor Patti *et al.*, alone or in combination, teach or suggest a pharmaceutical compositions comprising a therapeutically effective amount of a monoclonal antibody or an antigen binding fragment thereof that specifically binds to ribitol phosphate wall teichoic acid (WTA) of *S. aureus,* wherein said therapeutically effective amount of said antibody or fragment thereof alleviates or blocks colonization or infection by *S. aureus* upon administration to a patient.

In summary, Applicants respectfully submit that the claimed invention is not obvious in view of Fischer *et al.* and Patti *et al.* Thus, Applicants respectfully request that the rejection of claims 18, 21-25 and 28 be reconsidered and withdrawn.

SUMMARY

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicants' Attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

In addition, Applicants include herewith authorization to charge fees associated with new claims and the extension of time with which to respond, to Deposit Account No. 12-0080, under Order No. SYNI-007RCE2. The Director is also hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to Deposit Account No. 12-0080, under Order No. SYNI-007RCE2.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

By _____

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